Amendments to the Claims

The listing of claims set forth below will replace all prior versions and listings of claims in the application.

1. (Original) A method of decreasing coagulation or thrombosis in a system, comprising administering an ATIII molecule to the system, wherein the ATIII molecule has an increased affinity for heparin or heparan sulfate proteoglycans bound to a solid surface, and wherein the ATIII binds the heparin or heparan sulfate proteoglycans under high wall shear rate conditions with a higher affinity than alpha ATIII.

2. (Original) The method of claim 1, further comprising a determination that high wall shear rates on the ATIII will occur.

3. (Original) The method of claim 1, wherein the system comprises heparin or heparan sulfate proteoglycans attached to a solid surface.

4. (Original) The method of claim 1, wherein the system comprises a graft.

5. (Original) The method of claim 1, wherein the system comprises a catheter.

6. (Original) The method of claim 1, wherein the system comprises a medical device.

7. (Original) The method of claim 1, wherein the system comprises stent, a heart pump, a heart lung bypass machine, a blood oxygenator, a ventricular assist device, an extracorporeal circuit, a blood gas sensor, an intraocular lens, or a heparin coated thermoplastic.

8. (Original) The method of claim 1, wherein the ATIII comprises a beta ATIII.

9. (Original) The method of claim 1, wherein the dissociation constant of ATIII for heparin is from 0.1 nM to 300 nM.

10. (Original) The method of claim 1, wherein the dissociation constant of ATIII for heparin is less than or equal to 54 nM.

11. (Original) The method of claim 1, wherein the dissociation constant of ATIII for heparin is less than or equal to 6 nM.

12. (Original) The method of claim 1, wherein the dissociation constant of ATIII for heparin is less than or equal to 1 nM.

13. (Original) The method of claim 1, wherein the affinity of the ATIII for heparin is at least 5 times that of alpha ATIII.

14. (Original) The method of claim 1, wherein the affinity of the ATIII for heparin is at least 50 times that of alpha ATIII.

15. (Original) The method of claim 1, wherein the affinity of the ATIII for heparin is at least 250 times that of alpha ATIII.

16. (Original) The method of claim 1, wherein the ATIII is produced in an insect or yeast expression system.

17. (Original) The method of claim 1, wherein the solid surface comprises a biomaterial.

18. (Original) The method of claim 1, wherein the shear rate conditions comprise shear rates of at least 1000 sec^{-1}.

19. (Original) The method of claim 1, wherein the wall shear rate conditions comprise shear rates of at least 1500 sec^{-1}.

20. (Original) The method of claim 1, wherein the wall shear rate conditions comprise shear rates of at least 2000 sec^{-1}.

21. (Original) The method of claim 1, wherein the wall shear rate conditions comprise shear rates of at least 2500 sec^{-1}.

22. (Original) The method of claim 1, wherein the wall shear rate conditions comprise shear rates of at least 3000 sec^{-1}.

23. (Original) A method of inhibiting coagulation under low and high wall shear rate conditions comprising administering an ATIII molecule, wherein the ATIII molecule binds heparin or heparan sulfate proteoglycans under low and high wall shear rate conditions with an affinity higher than alpha ATIII.

24. (Original) The method of claim 23, wherein the wherein the ATIII comprises a beta ATIII.

25. (Original) The method of claim 23, wherein the dissociation constant of ATIII for heparin is from 0.1 nM to 300 nM.

26. (Original) The method of claim 23, wherein the dissociation constant of ATIII for heparin is less than or equal to 54 nM.

27. (Original) The method of claim 23, wherein the dissociation constant of ATIII for heparin is less than or equal to 6 nM.

28. (Original) The method of claim 23, wherein the dissociation constant of ATIII for heparin is less than or equal to 1 nM.

29. (Original) The method of claim 23, wherein the affinity of the ATIII for heparin is at least 5 times that of alpha ATIII.

30. (Original) The method of claim 23, wherein the affinity of the ATIII for heparin is at least 50 times that of alpha ATIII.

31. (Original) The method of claim 23, wherein the affinity of the ATIII for heparin is at least 250 times that of alpha ATIII.

32. (Original) The method of claim 23, wherein the ATIII is produced in an insect or yeast expression system.

33. (Original) The method of claim 23, wherein the shear rate conditions comprise shear rates of at least 1000 sec^{-1}.

34. (Original) The method of claim 23, wherein the shear rate conditions comprise shear rates of at least 1500 sec^{-1}.

35. (Original) The method of claim 23, wherein the shear rate conditions comprise shear rates of at least 2000 sec^{-1}.

36. (Original) The method of claim 23, wherein the shear rate conditions comprise shear rates

of at least 2500 sec^{-1}.

37. (Original) The method of claim 23, wherein the shear rate conditions comprise shear rates of at least 3000 sec^{-1}.

38. (Original) A method of inhibiting coagulation or thrombosis during or following a cardiovascular procedure on a subject comprising administering high affinity ATIII molecules to the subject, wherein the ATIII molecules bind heparin or heparan sulfate proteoglycans under low and high wall shear rate conditions with an affinity higher than alpha ATIII.

39. (Original) The method of claim 38, wherein the ATIII is administered upstream of the area where ATIII loading is desired.

40. (Original) The method of claim 38, wherein the wherein the ATIII comprises a beta ATIII.

41. (Original) The method of claim 38, wherein the dissociation constant of ATIII for heparin is from 0.1 nM to 300 nM.

42. (Original) The method of claim 38, wherein the dissociation constant of ATIII for heparin is less than or equal to 54 nM.

43. (Original) The method of claim 38, wherein the dissociation constant of ATIII for heparin is less than or equal to 6 nM.

44. (Original) The method of claim 38, wherein the dissociation constant of ATIII for heparin is less than or equal to 1 nM.

45. (Original) The method of claim 38, wherein the affinity of the ATIII for heparin is at least 5 times that of alpha ATIII.

46. (Original) The method of claim 38, wherein the affinity of the ATIII for heparin is at least 50 times that of alpha ATIII.

47. (Original) The method of claim 38, wherein the affinity of the ATIII for heparin is at least 250 times that of alpha ATIII.

48. (Original) The method of claim 38, wherein the ATIII is produced in an insect or yeast expression system.

49. (Original) The method of claim 38, further comprising administering heparin, heparan sulfate proteoglycans, or systemic anticoagulants.

50. (Currently Amended) A method of preconditioning a heparin or heparan sulfate ~~polyglycan~~ proteoglycan coated material, comprising incubating the material with a solution comprising ATIII molecules, such that the ATIII molecules bind to the heparin or heparan sulfate proteoglycans under low and high wall shear rate conditions with an affinity higher than alpha ATIII.

51. (Original) The method of claim 50, wherein the wherein the ATIII comprises a beta ATIII.

52. (Original) The method of claim 50, wherein the dissociation constant of ATIII for heparin is from 0.1 nM to 300 nM.

53. (Original) The method of claim 50, wherein the dissociation constant of ATIII for heparin is less than or equal to 54 nM.

54. (Original) The method of claim 50, wherein the dissociation constant of ATIII for heparin is less than or equal to 6 nM.

55. (Original) The method of claim 50, wherein the dissociation constant of ATIII for heparin is less than or equal to 1 nM.

56. (Original) The method of claim 50, wherein the affinity of the ATIII for heparin is at least 5 times that of alpha ATIII.

57. (Original) The method of claim 50, wherein the affinity of the ATIII for heparin is at least 50 times that of alpha ATIII.

58. (Original) The method of claim 50, wherein the affinity of the ATIII for heparin is at least 250 times that of alpha ATIII.

59. (Original) The method of claim 50, wherein the ATIII is produced in an insect or yeast

expression system.

60. (Original) A method of determining an amount of heparin or HSPG on a surface, the method comprising:

a. contacting the surface with a composition comprising an ATIII molecule at a wall shear rate, wherein the ATIII molecule has an increased affinity for heparin or heparan sulfate proteoglycans; and

b. assaying the amount of the ATIII molecule bound to the surface,

the amount of the ATIII bound to the surface being the minimum amount of heparin or heparan sulfate proteoglycan on the surface.

61. (Original) The method of claim 60, wherein the surface is contacted with an excess of the ATIII molecule, the amount of ATIII bound to the surface being the amount of heparin or heparan sulfate proteoglycan bound to the surface.

62. (Original) The method of claim 60, wherein the shear rate is 50, 630, 1500, or 3500 sec^{-1}.

63. (Original) The method of claim 60, wherein the wherein the ATIII comprises beta ATIII.

64. (Original) The method of claim 60, wherein the dissociation constant of ATIII for heparin is from 0.1 nM to 300 nM.

65. (Original) The method of claim 60, wherein the dissociation constant of ATIII for heparin is less than or equal to 54 nM.

66. (Original) The method of claim 60, wherein the dissociation constant of ATIII for heparin is less than or equal to 6 nM.

67. (Original) The method of claim 60, wherein the dissociation constant of ATIII for heparin is less than or equal to 1 nM.

68. (Original) The method of claim 60, wherein the affinity of the ATIII for heparin is at least 5 times that of alpha ATIII.

69. (Original) The method of claim 60, wherein the affinity of the ATIII for heparin is at

least 50 times that of alpha ATIII.

70. (Original) The method of claim 60, wherein the affinity of the ATIII for heparin is at least 250 times that of alpha ATIII.

71. (Original) The method of claim 60, wherein the ATIII is produced in an insect or yeast expression system.

72. (Original) A method of determining a wall shear rate on a heparin or HSPG coated surface, the method comprising:

a. contacting the surface with a composition comprising an ATIII molecule, wherein the ATIII molecule has an increased affinity for heparin or heparan sulfate proteoglycan; and

b. assaying the amount of ATIII bound to the surface,

the higher the amount of ATIII bound to the surface the higher the wall shear rate.

73. (Original) A method of coating a surface with heparin or heparan sulfate proteoglycan, the method comprising:

a. determining an amount of ATIII that binds to the surface, where the ATIII has a high affinity for heparin or heparan sulfate proteoglycan; and

b. coating the surface with heparin or heparan sulfate proteoglycan in an amount at least that of ATIII bound to the surface.

74. (Original) A variant of ATIII, comprising a substitution at Y131 or its positional equivilant.

75. (Original) The variant of claim 74, wherein the substitution at Y131 or its positional equivilant is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, lysine, leucine, methionine, serine, threonine, tryptophan, valine.

76. (Original) The variant of claim 74, wherein the substitution at Y131 or its positional

equivilant is leucine.

77. (Original) The variant of claim 74, wherein the substitution at Y131 or its positional equivilant is alanine.

78. (Original) The variant of claim 74, wherein the variant's affinity for heparin is at least 5 times that of alpha ATIII.

79. (Original) The variant of claim 74, wherein the variant's affinity for heparin is at least 50 times that of alpha ATIII.

80. (Original) The variant of claim 74, wherein the variant's affinity for heparin is at least 250 times that of alpha ATIII.

81. (Original) The variant of claim 74, wherein the dissociation constant for heparin is less than or equal to 1 nM.

82. (Original) An ATIII variant, wherein the heparin binding affinity and basal factor Xa rate are increased by disrupting interactions between helix D and sheet A of the native ATIII.